UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,368	12/12/2003	Craig A. Rosen	PZ045P1D1	2585

22195 7590 05/31/2006

HUMAN GENOME SCIENCES INC.
14200 SHADY GROVE ROAD
ROCKVILLE, MD 20850

EXAMINER	
JALLA, SANJOO	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,368	FISCELLA ET AL.	
	Examiner	Art Unit	
	Sanjoo Shree Jalla	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 3/20/06, is acknowledged.

   Claims 25-48 are under consideration in the instant application.

2. The request to change the Inventive entity to D.Roxanne Duan, Steven M. Ruben and Craig A. Rosen is hereby accepted.

3. It is noted that applicant has perfected the deposit requirement of the HCE3C63 cDNA contained in ATCC deposit No. PTA-909 in the parent application serial No. 09/832,129.

4. The U.S. Patent No. 6,936,691 cited on PTO-892 was issued from the parent Application No. 09/832,129.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

   The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

   Claims 25-48 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

   The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically: antibody or fragment thereof is useful for detecting or treating cancer in claims 25, 37 and 48.

   A review of the specification fails to reveal support for the new limitations.

   The specification as filed does not appear to provide a clear support for the limitation of claims 25, 37 and 48, where the antibody or fragment thereof is useful for detecting or treating cancer.

   Applicant has pointed to the support for the amendments made to claims 25, 37 and 48, in paragraphs 29-33, pages 10-13.

   Examiner's position is that the paragraphs 29-33, pages 10-13 does not support the amendment as recited because the instant disclosure at pages 10-13 discloses use of polypeptide for detecting or treating cancer and not antibody as claimed.

6. Claims 25-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the specification provides insufficient evidence for the claimed antibody or fragment thereof that specifically binds to a protein selected from the group consisting of: a) amino acids 34 to 766 of SEQ ID No: 35; b) amino acids 1 to 766 of SEQ ID No: 35; c) a mature portion of the HCE3C63 protein encoded by the HCE3C63 cDNA contained in ATCC Deposit No. PTA-909; and d) the full length HCE3C63 protein encoded by the HCE3C63 cDNA contained in ATCC Deposit No. PTA-909; wherein said antibody or fragment thereof is useful for detecting or treating any cancer.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art". The " amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The specification on page 11, asserts that polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue (s)or cell type(s). The specification points to Examples 11, 15 and 18 as exemplification for the use of protein in detection, treatment, and/or prevention of diseases (page 12) ranging from cancer to autism. A review of the examples does not support these assertions. Example 11 discloses the production of secreted proteins for high throughput screening assays, Example 15 discloses a high throughput-screening assay for identifying neuronal activity and Example 18 discloses a high throughput-screening assay for identifying changes in small molecule concentration and membrane permeability. It is unclear how any of these examples relate to the intended use of the antibody or fragment of protein of SEQ ID NO: 35. The specification does not disclose any particular disease condition wherein the claimed antibody detects. Clearly, these examples do not provide evidence of an antibody that is to be used for detecting and treating any cancer. Note that no data is provided to support any asserted function.

Further, treating cancer encompasses treating over 100 different diseases because cancer is a complex group of over 100 different diseases. Cancer can affect just about every organ in the human body and it is not clear how one antibody can detect and treat all the cancers for example,

breast cancer or leukemia or Hodgkins Lymphoma, etc. Duffy (Clinical Chemistry. 2005; 51: 494-503) in his review article notes that unpredictable efficacy and toxicity are hallmarks of most anticancer therapies. Duffy further notes that for malignancies other than breast cancers, validated predictive markers do not exist (see in particular abstract).

Thus, given the unpredictability of the art and the lack of working examples in the instant specification, one of ordinary skill in the art is not enabled to isolate an antibody or fragment thereof that specifically binds to a protein selected from the group consisting of: a) amino acids 34 to 766 of SEQ ID No: 35; b) amino acids 1 to 766 of SEQ ID No: 35; c) a mature portion of the HCE3C63 protein encoded by the HCE3C63 cDNA contained in ATCC Deposit No. PTA-909; and d) the full length HCE3C63 protein encoded by the HCE3C63 cDNA contained in ATCC Deposit No. PTA-909; wherein said antibody or fragment thereof is useful for detecting or treating any cancer. Therefore, the method of the claims cannot likely function as broadly claimed. Accordingly, given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 25-33, 35-44 and 46-48 stand rejected under 35 U.S.C. 103(a) as being unpatentable over EMBL accession number AL035289 (Rhodes, Jan- 1999) in view of Campbell (ed.), Monoclonal Antibody Technology, 1985; 2nd Edition as evidenced by Bost et. al. (Immunological Investigations, 1988; 17: 577-586).

AL035289 teaches a protein that has 72.6% identity with amino acid sequence of SEQ ID NO: 35 of instant application (see a copy of printout of the sequence alignment attached to the office action).

AL035289 does not teach specific antibodies or fragments thereof.

Campbell teaches that it is customary for any group working on protein to make monoclonal antibodies for basic research purposes (see in particular, Chapter 1, page 29, last paragraph). Further, as evidenced by Bost et.al., this antibody would be expected to cross react with other proteins. Bost et. al. teaches an antibody generated against HIV envelope protein that cross reacts with IL-2 even though the sequence homology between the two proteins is of 6 amino acids (see in particular abstract). Further, he teaches that these two peptides might be the cross-reactive epitopes (see in particular, page 584, lines 1-2).

Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to make an antibody as taught by Campbell to the protein as taught by

Rhodes that will cross react with protein of SEQ ID NO: 35 that has 72.6% homology with protein of Rhodes.

One of ordinary skill in the art at the time the invention was made would have been motivated to make antibodies (monoclonal, polyclonal or peptide) against the protein of Rhodes (that would also bind the protein of SEQ ID NO: 35) because antibodies are powerful immunochemical tools based on their specificity of binding, their homogeneity and their ability to be produced in large quantities (See in particular Campbell).

From combined teaching of the references, it is apparent that one of the ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Applicant's position is that examiner examines applicant's sequence alignment and informs Applicant if it significantly diverges from the sequence alignment recited by the Examiner.

Examiner's position as stated previously, is that, Rhodes et. al. teaches a protein that has 72.6% identity with amino acid sequence of SEQ ID NO: 35 of instant application (see a copy of printout of the sequence alignment attached to the office action) and as stated by Bost et.al., the antibody to this protein would be expected to cross react with other proteins. Bost et. al. teaches an antibody generated against HIV envelope protein that cross reacts with IL-2 even though the sequence homology between the two proteins is of 6 amino acids (see in particular abstract). Further, he teaches that these two peptides might be the cross-reactive epitopes (see in particular page 584, lines 1-2).

8. Claims 25-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over EMBL accession number AL035289 (Rhodes, Jan-1999) in view of Campbell (ed.), Monoclonal Antibody Technology, 1985; 2nd Edition, as evidenced by Bost et. al. (Immunological Investigations, 1988; 17: 577-586) as applied to claims 25-33, 35-44 and 46-48 above, and in further view of Owens et. al. (Journal of Immunological Methods. 1994; 168: 149-165), newly cited.

AL035289, Campbell and Bost et.al. have been discussed previously.

The combined references of AL035289 and Campbell do not teach the antibody to be either chimeric or humanized or single chain (claime 34 and 45) or a fragment (claims 25-48), such as a Fab fragment (claims 34 and 45).

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, and humanized antibodies. Owens *et al* further teach use of humanized antibodies in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments such as Fab fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement -dependent cytotoxcity (see in particular the entire document).

Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time

the invention was made to apply the teachings of Owens et.al. to the antibody of the combined teachings of Rhodes and Campbell to make a chimeric or humanized or single chain or a Fab fragment antibody.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimeric antibodies offer the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's position is that Gavilondo et. al. reference is not proper reference as it was published in July 2000 whereas the priority date of the present application is November 2, 1999.

Examiner has replaced Gavilondo et. al. reference with another reference by Owens et. al. that was published in 1994.

No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sanjoo Jalla whose telephone number is (571) 272-4453. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sanjoo Jalla, Ph.D.
Patent Examiner
Technology Center 1600
5/21/06

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600